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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,174	HANNA, NABIL	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/14/04, 12/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group 9 encompassing a part of claims 16, and 17, drawn to method of enhancing apoptosis by administering an immunoconjugate comprising an anti-CD20 antibody with IFN-alpha-2a and B-cell lymphoma cells as the elected species in the reply filed on 08/30/2004 is acknowledged. The traversal is on the ground(s) that examination of claims 1-6, directed to an immunoconjuate of the elected method of group 9 would not impose additional burden on the examiner. This is not found persuasive because searching the inventions of claims 1-6, drawn to multiple products, and group 9 drawn to method of using a fusion protein of an anti-CD 20 antibody linked to interferon-alpha-2a would impose serious search burden. The inventions of the multiple groups encompassed by claims 1-6, and the elected group 9 have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the multiple product and the method of enhancing apoptosis using the fusion product of anti-CD20 antibody linked to interferon alpha 2a are not coextensive. Claims 1-6 encompass multiple products. Prior art, which teaches one of products in claims 1-6 would not necessarily be applicable to the method of enhancing apoptosis in the elected group. Moreover, even if a product in claims 1-6 were known, the method of enhancing apoptosis using the product may be novel and unobvious in view of the preamble or active steps. As such, it would be burdensome to search the inventions of groups 9 and claims 1-6, drawn to multiple products together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-15, and 18-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/30/2004.

Claims 1-22 are pending. Claims 16, and 17 are examined as they read on the elected invention of method using an anti-CD20 antibody linked to IFN-alpha-2a (elected species) for enhancing apoptosis of B cell lymphoma (elected species)

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application i.e. PCT/US01/40835, specific reference to the earlier filed application must be made in the instant application. Note (37 CFR 1.78(a)(2) and (a)(5). For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet.

Claim Objections

Claims 16, and 17 are objected to because the claims are dependent on the non-elected claim. Appropriate correction is required.

For the purpose of this Office action, the limitation of claim 1 will be included in the examination of claims 16, and 17 as it read on the elected invention of method using an anti-CD20 antibody linked to IFN-alpha-2a (elected species).

Claims 16, and 17 are also objected to because the claims as currently construed are drawn to multiple inventions. The claims are not amended to reflect the applicant's election. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Demidem et al., Cancer Biother Radiopharm., June 1997, vol. 12, pages 177-186 in view of Hagenbeek et al., J Clin Oncol., January 1998, vol. 16 pages 41-47, further in view of Reff et al., 1994, Blood, vol. 83, pages 435-445.

Claims 16, and 17 are interpreted as drawn to method of enhancing apoptosis of lymphoma B cells using an immunoconjugate comprising an anti-CD20 antibody or a fragment thereof fused at its carboxy terminus to IFN-alpha-2a.

Demidem et al., teach that an anti-CD20 antibody enhances apoptosis of B lymphoma cells (note the title, and abstract), and also teach that pretreatment with the anti-CD20 antibody enhances cell killing of the target cells by other cytotoxic drugs.

Demidem et al., does not teach interferon alpha 2a as one of the other cytotoxic drugs.

However, Hagenbeek et al., teach that how to make and purify the human recombinant interferon alfa-2a had been known well before the effective filing date of the instant application. Hagenbeek et al., further teach that the human recombinant interferon alfa-2a has a good effect for patients with B cell lymphoma i.e. stages III and IV low-grade malignant non-Hodgkin's lymphoma (note the abstract).

Reff et al., 1994, Blood, vol. 83, pages 435-445 are cited to show the state of art of making a fusion protein of an anti-CD20 antibody or a fragment thereof fused at its carboxy terminus to IFN-alpha-2a. Reff et al., at Figs. 1 and 3 teach that how to construct a expression vector encoding anti-CD20 antibody, and also teach many useful restriction sites that could be used to fuse the human recombinant interferon alfa-2a.

Therefore it would have been obvious to one of the ordinary skill in the art to make and use an anti-CD20 antibody or a fragment thereof that is fused at its carboxy terminus to IFN-alpha-2a in the method of enhancing apoptosis in B cell lymphoma, thereby treating the lymphoma with a reasonable expectation of success since Hagenbeek et al., teach how to make recombinant interferon alfa-2a, and Reff et al., teach how to construct anti-CD20 antibody expression construct. One of an ordinary skill would have been motivated to make the fusion to minimize the painful injections by giving one fusion protein instead of two separate injections, and/or purifying one protein instead of two proteins, thus reducing cost and saving time.

Claims 16, and 17 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al., July 2000, Clinical Cancer Research, vol. 6, pages 2644-2652 in view of Taji et al., Jpn. J. Cancer Res., July 1998, vol. 89, pages 748-756.

Claims 16, and 17 are interpreted as drawn to method of enhancing apoptosis of lymphoma B cells using an immunoconjugate comprising an anti-CD20 antibody or a fragment thereof fused at its carboxy terminus to IFN-alpha-2a.

Davis et al., teach at page 2645, right column that an anti-CD20 antibody (i.e., Rituximab) and IFN had synergistic effect on preclinical trials, therefore the authors of the study set out to do the human clinical trials, and found that the combination therapy between anti-CD20 antibody, and interferon alpha 2a had a good result in humans as well.

Davis, et al., do not teach whether the good result is from enhancing apoptosis of the B lymphoma cells.

However, Taji et al., teach that an anti-CD20 antibody enhances apoptosis of B lymphoma cells (note the title and also Fig. 4 at page 752).

Therefore it would have been obvious to one of the ordinary skill in the art to make and use an anti-CD20 antibody or a fragment thereof is fused at its carboxy terminus to IFN-alpha-2a in the method of enhancing apoptosis in B cell lymphoma, thereby treating the lymphoma with a reasonable expectation of success since how to make recombinant interferon alfa-2a, and how to construct anti-CD20 antibody expression construct had been well known in the art before the effective filing date of the instant application. One of an ordinary skill would have been motivated to make the

fusion to minimize the painful injections by giving one fusion protein instead of two separate injections, and/or purifying one protein instead of two proteins, thus reducing cost and saving time.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642